IT IS CLAIMED:

1. A method of preparing lipid particles having an external lipid coating, comprising:

preparing lipid particles comprised of (i) a lipid composition containing a charged lipid and (ii) a therapeutic agent, said particles each having an outer lipid coating having an external lipid leaflet and an internal lipid structure; and

incubating said particles under conditions effective to remove said charged lipid from the external lipid leaflet.

2. The method of claim 1, wherein said preparing is comprised of preparing lipid particles composed of a lipid composition containing at least one cationic lipid.

3. The method of claim 1, wherein said preparing comprises (i) forming lipid vesicles composed of said lipid composition and (ii) complexing said lipid vesicles with said therapeutic agent.

4. The method of claim 1, wherein said incubating comprises incubating said lipid particles in a medium containing uncharged lipid vesicles.

5. The method of claim 4, wherein said incubating further includes adding to the medium a lipid-polymer-ligand conjugate.

6. The method of claim 1, wherein said lipid particles are liposomes.

7. The method of claim 6, wherein said incubating further includes adding to the medium a lipid derivatized with a hydrophilic polymer.

8. The method of claim 7 wherein said adding is comprised of adding a phospholipid derivatized with polyethyleneglycol.

9. The method of claim 1, wherein said incubating is at a temperature of

less than about 15 °C.

10. The method of claim 1, wherein said incubating is for a time of greater than about 5 hours.

11. The method of claim 1, wherein said preparing is comprised of preparing lipid particles having an entrapped therapeutic agent selected from the group consisting of a charged drug, a protein, a peptide, and a nucleic acid.

12. The method of claim 11, wherein said therapeutic agent is a protein or peptide.

13. A composition, comprising

lipid particles having a lipid coating comprised of an outer lipid leaflet and an inner lipid structure, said lipid coating formed of a lipid composition (i) comprising a charged lipid and (ii) having a gel-crystalline phase transition temperature, said lipid particles having no appreciable charge at a temperature lower than said phase transition temperature but having a measurable charge after incubation at a temperature above said phase transition temperature.

14. The composition of claim 13, wherein said lipid composition comprises a cationic lipid.

15. The composition of claim 13, wherein said lipid particles further include a therapeutic agent having a charge.

16. The composition of claim 15, wherein said therapeutic agent is a nucleic acid.

17. The composition of claim 15, wherein said lipid composition has a phase transition of between about 34-38 °C.

18. The composition of claim 15, wherein said lipid particles are liposomes.

19. A method of preparing lipid particles having an asymmetric charged lipid composition in its outer lipid coating prior to *in vivo* administration, comprising:

preparing lipid particles comprised of (i) a lipid composition containing a charged lipid and (ii) a therapeutic agent, said particles each having an outer lipid coating having an external lipid leaflet and an internal lipid structure; and

incubating said particles under conditions effective to remove charged lipids from the external lipid leaflet.

20. The method according to claim 19, wherein said incubating includes incubating at a temperature of less than about 15 °C.

21. The method according to claim 19, wherein said incubating includes incubating for a time of greater than about 5 hours.

22. The method according to claim 19, wherein said incubating includes incubating in a medium comprised of neutral lipid vesicles.